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09/539,032	03/30/2000	Samir Kumar Brahmachari	07064-01001	7985

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EXAMINER	
MORAN, MARJORIE A	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/539,032	Applicant(s) BRAHMACHARI ET AL.	
	Examiner Marjorie Moran	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-9 and species of M. tuberculosis, SEQ ID NO: 67, and DNA gyrase subunit B in Paper No. 12, filed 5/28/02 is acknowledged. The traversal is on the ground(s) that the invention is directed to a computer based method of identifying structural motifs, and is not limited to a specific microbe or microbial protein used. This is not found persuasive because while generic claim 1 does not recite specific microbes or proteins, dependent claims 3 and 6 clearly limit the method to one "using" specific microorganisms and proteins, from which the species were required to be elected in the office action of 11/15/01. The different microorganisms recited in claim 3 have different properties, growth characteristics, modes of infection, etc., and must be searched separately. The proteins recited in claim 6 are different structures, with different properties, and would be expected to behave differently in methods of use. As the species recited in claims 3 and 6 are patentably distinct and a search for any species would require a search different from that for any other species, the examiner maintains that the requirement for election of species of a microorganism and a protein is proper.

It is noted that applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, nor for requirement for election of a SEQ ID NO:

The requirement is still deemed proper for the reasons set forth above, and is therefore made FINAL.

Claims 10-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

An action on the merits of claims 1-9, as they read on the elected species, follows.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claim 6 is objected to because of the following informalities: Claim 6 recites "the said" in line 2, which is redundant. The examiner recommends deleting either "the" or "said" in line 2. Claim 6 also recites "said list of proteins comprise", which is grammatically incorrect. See also the rejection under 35 USC 112, below. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a LACK OF ENABLEMENT rejection.

The specification provides literal support for the language of the claims, on pages 7-10, but does not otherwise describe how to perform the claimed method. The specification teaches a method on pages 6-7 that describes how to perform the first six steps of the claimed method, wherein "common" peptides are designated as "invariant". It is not clear from the disclosure of

the specification if the "common" peptides are indeed invariant, or are merely conserved, as set forth below; however, for purposes of this rejection, the terms "invariant" and "conserved" as recited in the claims, are both interpreted to be the same as the "common" peptides taught on page 7 of the specification. After the step of computationally forming long common, or invariant peptide sequences, the specification discloses that conserved invariant peptides FROM THE SAME PROTEIN are clustered into one group, then the SECONDARY STRUCTURE of the protein is validated fro the crystal structures in the Protein Data Bank (PDB). The specification further discloses, on page 16, that a determination of whether a peptide sequence is present in a host is based on the identity and assigned function of the protein from which the invariant sequence is derived, not a comparison of all microbial genomes to a host genome. The specification further teaches comparison of peptide libraries from pathogenic versus nonpathogenic microorganisms, but does not teach a comparison of microbial genomes anywhere, thus there is no teaching anywhere for how to identify invariant PEPTIDE motifs by comparison of microbial GENOMES. There is no teaching anywhere in the specification for how to compare multiple pathogenic strain genomes to a host genome to select sequences not found in the host genome. The specification does not teach how to "validate" or identify invariant PEPTIDE motifs as potential drug targets by comparing any kind of GENOMIC data. The state of the prior art is such that methods to identify both peptide and nucleotide sequence motifs are known, as are methods of comparing sequences for similarity; e.g. to find conserved sequences (see WILBUR et al. PNAS (1983) vol. 80, pp. 726-730 and PIETROVSKI, Nucleic Acids Res. (1996) vol. 24 (19), pp. 3836-3845). However the prior art does not teach how to identify a peptide motif by comparison of genomic (nucleotide) sequences. It is well known in the art that there is redundancy in nucleotide coding for polypeptides, that introns and repetitive sequences are common in eukaryotic genomes, that a

single eukaryotic nucleotide sequence may encode a variety of proteins, or may not encode any protein (e.g. regulatory sequences), and that presence of a nucleotide motif does not necessarily correlate with a peptide motif. Although the level of skill in the art is acknowledged to be high, given the common knowledge in the art for the complexity and difficulty of predicting protein sequence and structure, if any, encoded by any particular eukaryotic genomic sequence, and the lack of teaching for how to do so by the instant specification, it would require undue experimentation by one skilled in the to determine whether a peptide motif may be useful as a drug target be determining if the peptide motif is present in a (eukaryotic) host by comparison of any or several microbial genomes with the host genome.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 6 contain an embedded hyperlink and/or other form of browser-executable code. An embedded hyperlink and/or other form of browser-executable code is an improper incorporation by reference, and therefore renders the claims indefinite. See MPEP § 608.01.

Claim 1 recites the term "the selected microbes" in step (i). There is no antecedent basis for this term in the claims, nor is any step of "selecting" microbes recited, therefore it is unclear which microbes from the database are intended to be "the selected microbes" and the claim is indefinite. This rejection may be overcome by deleting the term "the" before "microbes".

Claim 1 recites the term "the selected bacteria" in step (iii). There is no antecedent basis for this term in the claims. In addition, the use of two different terms: "microbes" in step (i) and

"bacteria" in step (iii) make its unclear whether applicant intends "the selected bacteria of step (iii) to be the same or a different set than the "selected microbes" of step (i). For these reasons, the claim is indefinite. If applicant intends the bacteria of step (iii) to be the same as the microbes of step (i), then this rejection may be overcome by replacing "bacteria" with -- microbes-- in step (iii).

Claim 1 recites "these conserved peptides" in step (vi). There is not antecedent basis for this term in the claims. Step (v) recites a step of obtaining a long chain of "invariant" peptide sequences; however, an "invariant" sequence is generally one which is identical from organism to organism, not merely conserved. For example, with regard to polynucleotide sequences, a "TATAA box" is a conserved regulatory region which comprises an invariant "TATAA" sequence - the rest of the sequence in the "box" may change slightly across a selection of organisms or genes, but must contain the exact sequence "TATAA". Applicant may be his own lexicographer; however in the case where a meaning attributed by applicant is different from that commonly accepted in the art, applicant must clearly set forth his intended meaning. The specification does not specifically define the term "invariant" anywhere, thus the examiner interprets "invariant" to have the commonly accepted meaning of "unchanging" and interprets "conserved" to have the commonly accepted meaning of "remaining constant but capable of slow change". Given these meanings, the long chain of "invariant" peptide sequences of step (v) is not an antecedent basis for "these conserved peptides" in step (vi).

Claim 1 recites the term "the invariant sequence motifs" in step (viii). There is no antecedent basis for this term in the claim, therefore the claim is indefinite. As set forth above, step (v) recites a step of obtaining a "long chain of invariant peptide sequences" but nowhere does the claim recite an "invariant sequence motif", nor is it clear whether the "long chain" of step (v) is a motif. Line 2 of step (viii) also recites the term "the given conserved sequences". It

is unclear whether applicant intends the antecedent basis for "the given conserved peptides" to be the "conserved peptides" of step (vi) or the "invariant sequence motif" recited earlier in step (viii), As set forth above, invariant sequences and conserved sequences are considered to be different in the art. It is recognized that conserved sequences or motifs may comprise invariant sequences, but it is unclear if this is applicant's intended meaning.

Claim 3 recites that protein sequence data is taken from any organism, but "not specifically limited to" particular microbes. As the claim is "not specifically" limiting the method, it is unclear what limitations applicant does intend, and the claim is indefinite.

Amended claim 4 recites limits "the conserved peptide motifs" of claim 1 "as modified"... Claim 1 does not recite any step of modification, therefore it is unclear what step of the method claim 4 is intended to modify. Further, there is no antecedent basis for "the conserved peptide motifs" in the claims. Parent claim 1 recites "invariant peptide motifs" in the preamble, and recites "invariant sequence motifs", "invariant peptide sequences", "conserved peptides", and "conserved sequences" in the claim steps, but does not recite "conserved peptide motifs" anywhere. For these reasons, claim 4 is indefinite.

Claim 4 recites "where ...peptide motifs as modified comprising...". This is an incorrect grammatical construction. Due to the claim language, it is unclear if application intends a further method step "comprising" modification of the recited peptides, or intends the peptide motifs to "comprise" one or more of the recited peptides. As the limitation intended by applicant is unclear, the claim is indefinite.

Claim 4 recites a limitation "comprising" a list of peptides, wherein the members of the list are not linked by a conjunction; e.g. either "and" or "or". It is therefore unclear if applicant intends a peptide to be one from the selected list, as would be indicted by inserting --or-- before the last member of the list; or intends the method to comprise (modification of?) all of the

peptides on the list, as would be indicted by inserting --and-- before the last member of the list. A method to comprising (modification of?) one or more members of a recited list is usually indicated the phrase --comprising one or more peptides from the group consisting of-- before the list. As it is unclear whether applicant intends the claimed method to be limited to one, all, or a subset of the recited peptides, the claim is indefinite. Applicant is reminded that amendments to the claims must be fully supported and enabled by the originally filed specification and/or claims.

Claim 5 limits the number of "invariant peptides". It is unclear what step or peptides of claim 1 applicant is intending to limit, therefore the claim is indefinite. Claim 1 recites identification of "invariant peptide motifs" in the preamble, and recites "validation" of "invariant sequence motifs" in step (viii), but does not recite "invariant peptides" anywhere. Sequences may contain short stretches of peptides which are invariant within a motif, therefore it is unclear if claim 5 is intended to limit the number of peptides within a motif, or is intended to limit the number of motifs identified or validated in the method of claim 1.

The preamble of claim 6 recites improper dependency in line 1; i.e. "the method as claimed in claim 1-4". As claims are required to recite dependency on multiple claims in the alternative, the phrasing of the preamble renders the claims indefinite. See MPEP 608.01 (n) and 37 CFR 1.75 (c). See the MPEP for examples of proper claim dependency language.

Claim 6 recites that a list of proteins "comprise", and recites a list wherein the members of the list are not joined by a conjunction. The combination of the term "comprise" and the lack of conjunction make it unclear whether applicant intends a list which --comprises-- all of the recited proteins, as would be indicated by the terms --comprises-- before the list and the term --and-- before the last member of the list; or intends the list to comprise proteins wherein the

proteins are selected from a recited list. As the limitation intended by applicant is unclear, the claim is indefinite.

Claims 7-9 recite claim limitations by reference to Figures. Reference to a figure, except in exceptional circumstances, is not a proper claim limitation, therefore the claims are rejected. See MPEP 2173.05 (s), which states: "Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993)." The Figures appear to be flowcharts representing a computer program or programs. As the steps and/or limitations of a computer program can usually be described with words and/or equations, it does not appear that it would be unduly difficult for applicant to define the invention represented by the flowcharts in words.

Conclusion

Claims 1-9 are rejected; claims 10-12 are withdrawn.

The prior art made of record and not relied upon which is considered pertinent to applicant's disclosure is MCGUIRE et al. (Genome Research (2000) vol. 10, pp. 744-757) who teaches discovery of motifs in microbial genomes, and BANSAL (Bioinformatics (1999) vol. 15 (11), pp. 900-908), who teaches comparative analysis of 17 microbial genomes found in the NCBI database to identify functional homologs.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to a patent analyst, Tina Plunkett, whose telephone number is (703) 305-3524.

Marjorie A. Moran
Examiner
Art Unit 1631

August 24, 2002